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NEWS 11 Apr 14 MEDLINE Reload
NEWS 12 Apr 17 Polymer searching in REGISTRY enhanced
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NEWS 18 May 15 Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19 May 19 Simultaneous left and right truncation added to WSCA
NEWS 20 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21 Jun 06 Simultaneous left and right truncation added to CBNB
NEWS 22 Jun 06 PASCAL enhanced with additional data
NEWS 23 Jun 20 2003 edition of the FSTA Thesaurus is now available
NEWS 24 Jun 25 HSDB has been reloaded
NEWS 25 Jul 16 Data from 1960-1976 added to RDISCLOSURE
NEWS 26 Jul 21 Identification of STN records implemented
NEWS 27 Jul 21 Polymer class term count added to REGISTRY
NEWS 28 Jul 22 INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available

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FILE COVERS 1907 - 23 Jul 2003 VOL 139 ISS 4
FILE LAST UPDATED: 22 Jul 2003 (20030722/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 11 and reductase
72580 REDUCTASE
5846 REDUCTASES
73531 REDUCTASE
(REDUCTASE OR REDUCTASES)

L3 9072 HMG?
2 L1 AND HMG?

=> S L1 and COA(W) reductase
35852 COA
827 COAS
36018 COA
(COA OR COAS)
72580 REDUCTASE
5846 REDUCTASES
73531 REDUCTASE
(REDUCTASE OR REDUCTASES)
7819 COA(W) REDUCTASE
L4 2 L1 AND COA(W) REDUCTASE

=> d 12 ibib abs hitstr tot

L2 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:334067 CAPLUS
DOCUMENT NUMBER: 135:225890
TITLE: Chromatographic purification of some
3-hydroxy-3-methylglutaryl coenzyme A
reductase inhibitors
AUTHOR(S): Grahek, R.; Milivojevic, D.; Bastarda, A.; Kracun, M.
CORPORATE SOURCE: Lek d.d., Research and Development, Ljubljana, 1526,
Slovenia
SOURCE: Journal of Chromatography, A (2001) 918(2), 319-324
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purifn. of pravastatin, simvastatin and lovastatin in the sodium salt
or lactone form and of mevastatin in the lactone form by reversed-phase
displacement chromatog. is presented. The mobile phases
consisted of water or mixts. of water-methanol and water-acetonitrile.
Six different displacers were successfully used. Up to 0.14 g of raw
sample per g of stationary phase was loaded on a column packed with
silica-based octadecyl phase. Crude substances from 85 to 88% chromatog.
purity were purified and at least 99.5% purity was achieved.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:210141 CAPLUS
DOCUMENT NUMBER: 132:241979
TITLE: Process for obtaining HMG-CoA reductase
inhibitors of high purity
INVENTOR(S): Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej
PATENT ASSIGNEE(S): Lek Pharmaceutical and Chemical Company D.D., Slovenia
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017182	A1	20000330	WO 1999-IB1553	19990917

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,

MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
SI 20072 C 20000430 SI 1998-241 19980918
CA 2343645 AA 20000330 CA 1999-2343645 19990917
AU 9955284 A1 20000410 AU 1999-55284 19990917
EP 1114040 A1 20010711 EP 1999-941797 19990917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO
JP 2002526486 T2 20020820 JP 2000-574092 19990917
HR 2001000045 A1 20011231 HR 2001-45 20010116
BG 105348 A 20011130 BG 2001-105348 20010316
PRIORITY APPLN. INFO.: SI 1998-241 A 19980918
WO 1999-IB1553 W 19990917

AB Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and
derivs. and analogs are known as HMG-CoA **reductase** inhibitors
and are used as antihypercholesterolemic agents. The majority of them are
produced by fermn. using microorganisms of different species identified as
species belonging to Aspergillus, Monascus, Nocardia, Amycolatopsis, Mucor
or Penicillium genus, some are obtained by treating the fermn. products
using the method of chem. synthesis or they are the products of total
chem. synthesis. The purity of the active ingredient is an important
factor for manufg. the safe and effective pharmaceutical, esp. if the
pharmaceutical product must be taken on a longer term basis in the
treatment or prevention of high plasma cholesterol. The accumulation of
the impurities from the pharmaceuticals of lower purity may cause many
side effects during the medical treatment. The present invention relates
to a new industrial process for the isolation of HMG-CoA **reductase**
inhibitors using so-called **displacement chromatog.**

Use of the invention enables to obtain HMG-CoA **reductase**
inhibitors of high purity, with high yields, lower prodn. costs and
suitable ecol. balance. Crude sodium salt of pravastatin (HPLC purity
88%) was dissolved in the mobile phase A (distd. water), pH was adjusted
to 7 with 0.2M aq. NaOH soln. and filtered. The column was equilibrated
with mobile phase A. The sample obtained in the above manner was fed onto
the Grom-Sil 120-ODS HE column (particle size 30 11 .mu.m, column size 250
x 10 mm). The column was washed with the mobile phase B contg. 7% of
diethylene glycol monobutyl ether in mobile phase A at the flow rate of
4.5 mL/min. Absorbance was measured at 260 nm, and the 0.5 mL fractions
were collected with an initial increase in the absorbance. When the
signal decreased the column was washed with 25 mL of 70% MeOH. The
fractions obtained were analyzed by the HPLC method. The fractions with a
purity 99.5% were pooled. In the pooled fractions (7 mL), the HPLC purity
was 99.8%.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:210141 CAPLUS
DOCUMENT NUMBER: 132:241979
TITLE: Process for obtaining HMG-CoA reductase
inhibitors of high purity
INVENTOR(S): Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej
PATENT ASSIGNEE(S): Lek Pharmaceutical and Chemical Company D.D., Slovenia
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017182	A1	20000330	WO 1999-IB1553	19990917
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SI 20072	C	20000430	SI 1998-241	19980918
CA 2343645	AA	20000330	CA 1999-2343645	19990917
AU 9955284	A1	20000410	AU 1999-55284	19990917
EP 1114040	A1	20010711	EP 1999-941797	19990917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526486	T2	20020820	JP 2000-574092	19990917
HR 2001000045	A1	20011231	HR 2001-45	20010116
BG 105348	A	20011130	BG 2001-105348	20010316
PRIORITY APPLN. INFO.:			SI 1998-241	A 19980918
			WO 1999-IB1553	W 19990917

AB Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and derivs. and analogs are known as **HMG-CoA** reductase inhibitors and are used as antihypercholesterolemic agents. The majority of them are produced by fermn. using microorganisms of different species identified as species belonging to *Aspergillus*, *Monascus*, *Nocardia*, *Amycolatopsis*, *Mucor* or *Penicillium* genus, some are obtained by treating the fermn. products using the method of chem. synthesis or they are the products of total chem. synthesis. The purity of the active ingredient is an important factor for manufg. the safe and effective pharmaceutical, esp. if the pharmaceutical product must be taken on a longer term basis in the treatment or prevention of high plasma cholesterol. The accumulation of the impurities from the pharmaceuticals of lower purity may cause many side effects during the medical treatment. The present invention relates to a new industrial process for the isolation of **HMG-CoA** reductase inhibitors using so-called **displacement chromatog.** Use of the invention enables to obtain **HMG**-CoA reductase inhibitors of high purity, with high yields, lower prodn. costs and suitable ecol. balance. Crude sodium salt of pravastatin (HPLC purity 88%) was dissolved in the mobile phase A (distd. water), pH was adjusted to 7 with 0.2M aq. NaOH soln. and filtered. The column was equilibrated with mobile phase A. The sample obtained in the above manner was fed onto the Grom-Sil 120-ODS HE column (particle size 30 11 .mu.m, column size 250 x 10 mm). The column was washed with the mobile phase B contg. 7% of diethylene glycol monobutyl ether in mobile phase A at the flow rate of 4.5 mL/min. Absorbance was measured at 260 nm, and the 0.5 mL fractions were collected with an initial increase in the absorbance. When the signal decreased the column was washed with 25 mL of 70% MeOH. The fractions obtained were analyzed by the HPLC method. The fractions with a purity 99.5% were pooled. In the pooled fractions (7 mL), the HPLC purity was 99.8%.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1982:449945 CAPLUS

DOCUMENT NUMBER: 97:49945

TITLE: Identification of protein(s) secreted by the preovulatory ovary which suppresses the follicle response to gonadotropins

AUTHOR(S): DiZerega, Gere S.; Goebelmann, Uwe; Nakamura, Robert M.

CORPORATE SOURCE: Sch. Med., Univ. Southern California, Los Angeles, CA, 90033, USA

SOURCE: Journal of Clinical Endocrinology and Metabolism (1982), 54(6), 1091-6

CODEN: JCEMAZ; ISSN: 0021-972X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ovarian venous blood (5 mL) was collected from women undergoing laparotomy for indications not related to ovarian dysfunction on days 12-14 after the onset of their last menstrual period. Serum was fractionated by (NH4)2SO4 pptn., dialyzed against buffer with 10,000 mol. wt. exclusion membranes, and thereafter sequentially eluted through concanavalin A and Sephadex G-50 columns. The activity of the eluent was assessed as inhibition of ovarian wt. increase and serum 17.beta.-estradiol [50-28-2] levels in 23-day-old, hypophysectomized, diethylstilbestrol-treated rats (HIFR) challenged with human menopausal gonadotropin (hMG) [61489-71-2]. Sephadex G-50 fractions (elution vol./void vol. 1.42-1.55) from patient 1 produced a decrease in ovarian wt. (59 vs. 89.1 g) and a decrease in serum 17.beta.-estradiol levels (<25 vs. 215.5 pg/mL). Although peripheral and ovarian venous blood collected from the ovary contralateral to the site of ovulation demonstrated similar Sephadex G-50 elution profiles, when representative fractions were tested by bioassay, no redn. in ovarian wt. or serum 17.beta.-estradiol levels was found. In addn., ovarian venous serum from the ovulatory ovary of patients 2 and 3 had a similar Sephadex G-50 elution profile with fractions (elution vol./void vol. = 1.48-1.60) which suppressed rat ovarian wt. and serum 17.beta.-estradiol concns. in the hMG-HIFR assay. When active fractions from the G-50 eluents were heated to 56.degree. or trypsin digested, they lost their ability to suppress ovarian wt. and 17.beta.-estradiol secretion in response to hMG stimulation. Estns. of mol. wt. by gel permeation ranged 14,000-18,000 for patients 1-3. Bioassay results from representative fractions obtained by ampholyte displacement chromatog. suggested that the isoelec. point of active material was pH, 5.8-6.5 for patients 1-3. Similarly processed samples from 3 anovulatory patients contained no inhibitory activity in the bioassay. Thus, the identification of a heat- and trypsin-labile substance secreted directly into the venous drainage from the ovary contg. the dominant follicle which suppresses the follicular response to gonadotropins is reported. That this protein is not secreted in large amts. by anovulatory ovaries was evidenced by the failure of the bioassay to detect inhibitory activity in the venous drainage of the contralateral ovary of patients 1-3 as well as the ovarian venous effluents from 3 anovulatory women.

=> d 14 ibib abs hitstr tot

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:334067 CAPLUS
DOCUMENT NUMBER: 135:225890
TITLE: Chromatographic purification of some 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors

AUTHOR(S): Grahek, R.; Milivojevic, D.; Bastarda, A.; Kracun, M.
CORPORATE SOURCE: Lek d.d., Research and Development, Ljubljana, 1526, Slovenia

SOURCE: Journal of Chromatography, A (2001), 918(2), 319-324

CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purifn. of pravastatin, simvastatin and lovastatin in the sodium salt or lactone form and of mevastatin in the lactone form by reversed-phase **displacement chromatog.** is presented. The mobile phases consisted of water or mixts. of water-methanol and water-acetonitrile. Six different displacers were successfully used. Up to 0.14 g of raw sample per g of stationary phase was loaded on a column packed with silica-based octadecyl phase. Crude substances from 85 to 88% chromatog. purity were purified and at least 99.5% purity was achieved.

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L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:210141 CAPLUS
DOCUMENT NUMBER: 132:241979
TITLE: *Process for obtaining HMG-CoA reductase inhibitors of high purity*
INVENTOR(S): Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej
PATENT ASSIGNEE(S): Lek Pharmaceutical and Chemical Company D.D., Slovenia
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SI 20072	C	20000430	SI 1998-241	19980918
CA 2343645	AA	20000330	CA 1999-2343645	19990917
AU 9955284	A1	20000410	AU 1999-55284	19990917
EP 1114040	A1	20010711	EP 1999-941797	19990917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526486	T2	20020820	JP 2000-574092	19990917
HR 2001000045	A1	20011231	HR 2001-45	20010116
BG 105348	A	20011130	BG 2001-105348	20010316
PRIORITY APPLN. INFO.:			SI 1998-241	A 19980918
			WO 1999-IB1553	W 19990917

AB Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and derivs. and analogs are known as HMG-CoA **reductase** inhibitors and are used as antihypercholesterolemic agents. The majority of them are produced by fermn. using microorganisms of different species identified as species belonging to *Aspergillus*, *Monascus*, *Nocardia*, *Amycolatopsis*, *Mucor* or *Penicillium* genus, some are obtained by treating the fermn. products using the method of chem. synthesis or they are the products of total chem. synthesis. The purity of the active ingredient is an important factor for manufg. the safe and effective pharmaceutical, esp. if the pharmaceutical product must be taken on a longer term basis in

the treatment or prevention of high plasma cholesterol. The accumulation of the impurities from the pharmaceuticals of lower purity may cause many side effects during the medical treatment. The present invention relates to a new industrial process for the isolation of HMG-CoA **reductase** inhibitors using so-called **displacement chromatog.** Use of the invention enables to obtain HMG-CoA **reductase** inhibitors of high purity, with high yields, lower prodn. costs and suitable ecol. balance. Crude sodium salt of pravastatin (HPLC purity 88%) was dissolved in the mobile phase A (distd. water), pH was adjusted to 7 with 0.2M aq. NaOH soln. and filtered. The column was equilibrated with mobile phase A. The sample obtained in the above manner was fed onto the Grom-Sil 120-ODS HE column (particle size 30 11 .mu.m, column size 250 x 10 mm). The column was washed with the mobile phase B contg. 7% of diethylene glycol monobutyl ether in mobile phase A at the flow rate of 4.5 mL/min. Absorbance was measured at 260 nm, and the 0.5 mL fractions were collected with an initial increase in the absorbance. When the signal decreased the column was washed with 25 mL of 70% MeOH. The fractions obtained were analyzed by the HPLC method. The fractions with a purity 99.5% were pooled. In the pooled fractions (7 mL), the HPLC purity was 99.8%.

REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT